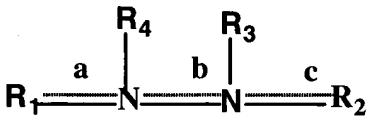
Appendix 1 – Pending Claims

1. A method of reducing mortality associated with heart failure, for improving the oxygen consumption, for improving the quality of life or for improving exercise tolerance in a black patient comprising administering to the black patient a therapeutically effective amount of at least one hydralazine compound of Formula (I) or a pharmaceutically acceptable salt thereof, and at least one of isosorbide dinitrate and isosorbide mononitrate,

wherein the hydralazine compound of Formula (I) is

(I)



wherein a, b and c are each independently a single or a double bond; R_1 and R_2 are each independently a hydrogen, an alkyl, an ester or a heterocyclic ring; R_3 and R_4 are each independently a lone pair of electrons or a hydrogen, with the proviso that at least one of R_1, R_2, R_3 and R_4 is not a hydrogen.

2. The method of claim 1, wherein the black patient has a less active renin-angiotensin system relative to a white patient.

3. The method of claim 1, wherein the black patient has hypertension.

4. The method of claim 1, further comprising administering a pharmaceutically acceptable carrier.

5. The method of claim 1, wherein the hydralazine compound is budralazine, cadralazine, dihydralazine, endralazine, hydralazine, pildralazine, todralazine or a pharmaceutically acceptable salt thereof.

6. The method of claim 5, wherein the hydralazine compound is hydralazine hydrochloride.

7. The method of claim 6, wherein the hydralazine hydrochloride is administered in an amount of about 30 milligrams per day to about 300 milligrams per day.

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8. The method of claim 1, wherein the isosorbide dinitrate is administered in an amount of about 20 milligrams per day to about 200 milligrams per day.

9. The method of claim 1, wherein the isosorbide mononitrate is administered in an amount of about 10 milligrams per day to about 120 milligrams per day.

10. The method of claim 1, comprising administering at least one hydralazine compound or a pharmaceutically acceptable salt thereof and isosorbide dinitrate.

11. The method of claim 1, comprising administering at least one hydralazine compound or a pharmaceutically acceptable salt thereof and isosorbide mononitrate.

12. The method of claim 1, comprising administering at least one hydralazine compound or a pharmaceutically acceptable salt thereof, isosorbide dinitrate and isosorbide mononitrate.

13. The method of claim 1, wherein the at least one hydralazine compound and the at least one of isosorbide dinitrate and isosorbide mononitrate are administered orally.

14. The method of claim 13, wherein the at least one hydralazine compound and the at least one of isosorbide dinitrate and isosorbide mononitrate are orally administered in the form of a solid dose.

15. The method of claim 14, wherein the solid dose is in the form of a tablet or a capsule.

16. The method of claim 15, wherein the capsule is in the form of a sustained release capsule

17. The method of claim 15, wherein the tablet is in the form of a sublingual tablet, a sustained-release tablet or a chewable tablet.

18. The method of claim 1, wherein the at least one hydralazine compound and the at least one of isosorbide dinitrate and isosorbide mononitrate are administered to the black patient as components of the same composition.

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19. The method of claim 1, wherein the at least one hydralazine compound and the at least one of isosorbide dinitrate and isosorbide mononitrate are administered to the black patient as separate components.

20. The method of claim 19, wherein the at least one hydralazine compound and the at least one of isosorbide dinitrate and isosorbide mononitrate are administered to the black patient as separate components at about the same time.

21. The method of claim 1, further comprising administering a digitalis.

22. The method of claim 21, wherein the digitalis is digoxin

23. The method of claim 22, wherein the digoxin is administered in an amount to achieve a blood serum concentration of at least about 0.7 nanograms per milliliter to about 2.0 nanograms per milliliter.

24. The method of claim 1, further comprising administering an effective edema managing amount of a diuretic compound.

25. The method of claim 24, wherein the diuretic compound is a thiazide, ethacrynic acid, a furosemide, a spiranolactone, a triamterene or a mixture thereof.

26. The method of claim 24, further comprising administering potassium.

27. The method of claim 26, wherein the potassium is administered in the form of potassium chloride or by the daily ingestion of foods with high potassium content.

28. The method of claim 1, further comprising administering at least one compound used to treat a cardiovascular disease.

29. The method of claim 28, wherein the at least one compound used to treat a cardiovascular disease is an angiotensin-converting enzyme inhibitor, a beta-adrenergic blocker, a cholesterol reducer, a calcium channel blocker, an angiotensin II receptor antagonist, an endothelin antagonist, or a mixture thereof.

30. The method of claim 29, wherein the angiotensin-converting enzyme inhibitor is alacepril, benazepril, captopril, ceronapril, cilazapril, delapril, enalapril, enalaprilat, fosinopril,

imidapril, lisinopril, moveltipril, pentopril, perindopril, quinapril, ramipril, rentiapril, spirapril, temocapril, trandolapril, zofenopril, or a mixture thereof.

31. The method of claim 30, wherein the angiotensin-converting enzyme inhibitor is enalapril.

32. (Amended) A method of reducing the incidence of mortality associated with chronic congestive heart failure in a patient with impaired cardiac function and concomitant reduced exercise tolerance, comprising orally administering to said patient between about 30 and about 300 milligrams of hydralazine hydrochloride per day, and at least one of (i) between about 20 and about 200 milligrams of isosorbide dinitrate, per day, and (ii) between about 10 and about 120 milligrams of isosorbide mononitrate, per day wherein the improvement comprises administering the hydralazine hydrochloride and the at least one of isosorbide dinitrate and isosorbide mononitrate to a black patient.

33. The method of claim 32, further comprising treating the black patient orally with digoxin in an amount sufficient to achieve a blood serum concentration of digoxin of at least about 0.7 nanograms per milliliter and an effective edema managing amount of at least one pharmaceutically acceptable diuretic selected from a thiazide, a ethacrynic acid, a furosemide, a spironalactone and a triamterene.

34. The method of claim 33, further comprising administering potassium.

35. The method of claim 32, further comprising treating the black patient with at least one compound used to treat a cardiovascular disease.

36. The method of claim 35, wherein the at least one compound used to treat a cardiovascular disease is an angiotensin-converting enzyme inhibitor, a beta-adrenergic blocker, a cholesterol reducer, a calcium channel blocker, an angiotensin II receptor antagonist, an endothelin antagonist, or a mixture thereof.

37. The method of claim 36, wherein the angiotensin-converting enzyme inhibitor is alacepril, benazepril, captopril, ceronapril, cilazapril, delapril, enalapril, enalaprilat, fosinopril, imidapril, lisinopril, moveltipril, pentopril, perindopril, quinapril, ramipril, rentiapril, spirapril, temocapril, trandolapril, zofenopril, or a mixture thereof.

38. The method of claim 37, wherein the angiotensin-converting enzyme inhibitor is enalapril.

42 The method of claim 1, wherein the black patient is not as responsive to an angiotensin-converting enzyme inhibitor relative to a white patient.

43. The method of claim 1, wherein the black patient has a deficient nitric oxide generation system.

44. The method of claim 32, wherein the black patient is not as responsive to an angiotensin-converting enzyme inhibitor relative to a white patient.

45. The method of claim 32, wherein the black patient has a deficient nitric oxide generation system.

46. The method of claim 32, wherein the black patient has a less active renin-angiotensin system relative to a white patient.

47. The method of claim 32, wherein the black patient has hypertension.

48. A method of reducing mortality associated with heart failure in a black patient comprising administering to the black patient a therapeutically effective amount of hydralazine or a pharmaceutically acceptable salt thereof and isosorbide dinitrate.

49. A method of reducing mortality associated with heart failure in a black patient with hypertension comprising administering to the black patient with hypertension a therapeutically effective amount of hydralazine or a pharmaceutically acceptable salt thereof and isosorbide dinitrate.

~~51.~~ 47 (New) The method of claim 32, wherein the hydralazine hydrochloride and the at least one of isosorbide dinitrate and isosorbide mononitrate are administered orally.

~~52.~~ 48 (New) The method of claim ~~51~~ 47, wherein the hydralazine hydrochloride and the at least one of isosorbide dinitrate and isosorbide mononitrate are orally administered in the form of a solid dose.

~~53.~~ 49 (New) The method of claim ~~52~~ 48, wherein the solid dose is in the form of a tablet or a capsule.

~~54~~ 50. (New) The method of claim ~~53~~ 49, wherein the capsule is in the form of a sustained release capsule.

~~55~~ 51. (New) The method of claim ~~53~~ 49, wherein the tablet is in the form of a sublingual tablet, a sustained-release tablet or a chewable tablet.

~~56~~ 52. (New) The method of claim 32, wherein the hydralazine hydrochloride and the at least one of isosorbide dinitrate and isosorbide mononitrate are administered to the black patient as components of the same composition.

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~~57~~ 53. (New) The method of claim 32, wherein the hydralazine hydrochloride and the at least one of isosorbide dinitrate and isosorbide mononitrate are administered to the black patient as separate components.

~~58~~ 54. (New) The method of claim ~~57~~ 53, wherein the hydralazine hydrochloride and the at least one of isosorbide dinitrate and isosorbide mononitrate are administered to the black patient as separate components at about the same time.